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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,889	09/20/2005	Federico Arcamone	833-132 US	2682

26817 7590 01/16/2008
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EXAMINER
BARKER, MICHAEL P

ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
01/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,889	ARCAMONE ET AL.	
	Examiner	Art Unit	
	Michael P. Barker	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03/05/2007, Preliminary Amendment*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6-8* is/are rejected.

7)☒ Claim(s) *2-7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/29/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 are pending in this Application.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on July 17, 2006 was correctly filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the/ IDS was considered by the Examiner. Please refer to Applicant's copy of PTO-1449, submitted herewith.

Claim Rejections - 35 USC § 112 ¶1

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and **7** are rejected under 35 USC 112 ¶1 paragraph as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it

> obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

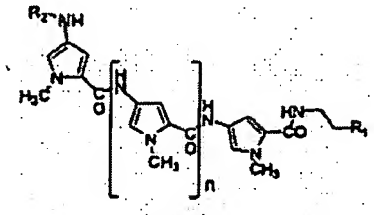
Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what does not constitute a representative number of species to adequately describe a broad genus. For example, in *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The Guidelines for Examination of Patent Applications Under 35 USC 112, ¶1, "Written Description" Requirement (Federal Register, Vol. 66, No. 4, pg. 1105, column 3), in accordance with MPEP § 2163, specifically state that for each claim drawn to a genus, the written description requirement may be satisfied through a sufficient description of a representative number of species by **a)** actual reduction to practice; **b)** reduction to drawings or structural chemical formulas; **c)** disclosure of relevant, identifying characteristics (i.e. structure) by functional characteristics coupled with a known or disclosed correlation between function and structure. The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention (Federal Register, Vol. 66, No. 4, p. 1105, 3rd column, 3rd paragraph).

Scope of Claims



I (n=0,1)

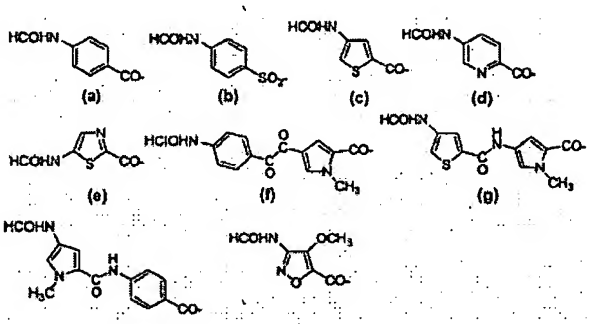
Compounds of the general formula, . The following moieties are claimed *broader* than what is supported by the scope of the disclosure:

- R_1; and
- R_2.

Scope of Disclosure

Reduction to Practice:

The compounds reduced to practice in the art support the following definitions of the aforementioned moieties:

- $\mathbf{R_1}$ is -C(NH)NH$_2$, -C(NH)NHR$_3$, -NH2, NHR$_3$ -N(R$_3$)$_2$, -NR$_3$R$_4$, -NH-C(NH)NH$_2$, -NH-C(NH)NHR$_3$, -N(CH$_2$)$_4$, N(R$_3$)$_3$+ ; and
- $\mathbf{R_2}$ is  and OHCHN-.

Reduction to Structural or Chemical Formulas:

The only disclosure, in addition to the species reduced to practice, is in form of a *list* or "genus" (e.g. $\mathbf{R_1}$ and $\mathbf{R_2}$) of possible substituents for the moieties. This type of disclosure is not viewed to be sufficient to claim every of structure encompassed by $\mathbf{R_1}$ and $\mathbf{R_2}$ (e.g. $\mathbf{R_1}$ is any functional group, and $\mathbf{R_2}$ is any aliphatic, aromatic, or arylaliphatic acyclic group) A "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species. MPEP 2163.I.A. and *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39

USPQ2d 1895, 1905 (Fed. Cir. 1996). Therefore, there is no disclosure of species (e.g. by reduction to structural/chemical formulas) in addition to those reduced to practice, listed above.

Correlation between Structure and Function:

Structure-activity studies are disclosed in the art for anti-bacterial/anti-fungal compounds and compositions for genuses of compounds different from those instantly claimed. Although these studies do not address the activity of the compounds of the instant genus as a function of structural modifications, they do show that a compound's ability to treat specific viral, bacterial, and protozoarian infections is influenced by structural changes to the common chemical core. Because the instant specification does not disclose any correlation between function and structure, and because such correlation does not exist in the art for the instantly claimed genus of compounds, one of ordinary skill would not know what *specific structural elements* are *essential* for the activity of the instantly claimed compounds.

Analysis of Fulfillment of Written Description Requirement:

In the absence of a correlation between structure and function, it is not possible to know what modifications to the instantly claimed core structure will allow for the preservation of the desired activity. For example, one of ordinary skill cannot predict whether the activity will be preserved upon changing the aforementioned moieties to result in a compound unrepresented by the instant disclosure.

In conclusion: (i) substantial structural variation exists in the genus/subgenus embraced by **Claims 1-3** and **7**; (ii) disclosure of species-supporting genus is limited to compounds reduced to practice, which scope is not commensurate with the scope of genus/subgenus claimed; and (iii) common structural attributes of the claimed genus/subgenus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art. Thus, the specification fails to provide adequate written description for the genus of compounds claimed and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections – 35 USC 103(a)

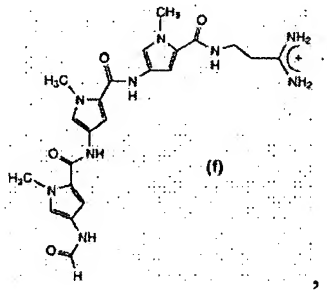
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4 and **6-8** are rejected under 35 U.S.C. 103(a) as being unpatentable over Cortesi, et al., *Drug Discovery Today*, Vol. 6, Issue 17, pp. 893-904 (1 September 2001) and U.S. Patent No. 6,120,797 (19 Sept. 2000).

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

Cortesi, et al. (hereinafter, "Cortesi") discloses at least one compound which falls within the scope of the generic lextriposins of **Claim 1** (e.g. the specific lexitropsin of instant **Claim 4**), namely, 

, distamycin A [p. 894, Fig. 1, compound (f)] . Cortesi states that distamycin binds to DNA (a.k.a. a DNA Binding Drug – "DBD"), preventing binding of nuclear proteins to their specific target sequences and forms a noncovalent complex with DNA via binding to the groove. (pp. 893 and 895). Distamycin is a known antitumor-antibiotic which belongs to a class of minor-groove alkylating compounds which are able to bind reversibly to DNA with high selectivity for AT-rich sequences and shows antiviral and antiprotozoal activity.

According to Cortesi, during the past decade, there has been an increasing focus on the search for methods to target specifically antitumor agents to the tumor site, prompted by the lack of tumor specificity of systemically administered antitumor drugs (including distamycin). (p. 897). One approach offered to overcome this lack of tumor specificity was offered by drug delivery systems (hereinafter "DDSs"), such as polymers, liposomes, nanoparticles, microparticles, as well as bacterial and cellular ghosts, which can reach the tumor site more efficiently and more selectively than the drugs alone. *Id.* Cortesi goes on to state that a range of materials has been employed to control the release of drugs and other active ingredients, such as

polymers designed primarily for medical application, i.e. polylactides, polyglycolides, poly (lactide-co-glycolides), polyanhydrides, and polyorthoesters. *Id.* One advantage of using such polymers is their biodegradability, guaranteeing their degradation into nontoxic molecules which can be excreted through normal metabolic pathways making it unnecessary to remove the implanted DDSs after complete delivery of the drug. *Id.* Another advantage of this type of DDS lies in the fact that the DDS lessens the toxicity of the drugs to areas other than the selected target. (pp. 895-898).

Cortesi notes that the aforementioned types of DDSs have been applied to DBDs, such as cisplatin. (p. 897). Liposomal formulations have been proposed for the administration of cisplatin to overcome the toxicity and drug resistance currently associated with cisplatin. *Id.* For instance, Aroplatin™ is a liposomal formulation that can be used to administer cisplatin intrapleurally in the treatment of lung cancer, as well as several solid tumors, such as renal cell carcinoma. *Id.* In addition, SPT-077 is a long-acting 'stealth' liposome formulation for cisplatin. Stealth technology uses polyethylene glycol (PEG) to prevent the body's natural defense mechanism from rupturing the liposomes, thereby increasing their circulation time. (p. 898).

Cortesi also notes that nanoparticulate carriers have been considered for improving the pharmacokinetic and pharmacodynamic profile of certain DBDs. (p. 900). Another DDS reported is the incorporation of a DBD into polymeric micelles based on poly(ethylene glycol)-poly(aspartic acid) block copolymer.

U.S. Patent No. 6,120,797 discloses liposomes containing one or more N-acylated phosphatidylethanolamines (PE) as useful for the localization of delivering bioactive agents, such as antiviral agents and antibacterial agents, to cells. (Abstract and col. 8). The '797 Patent

discloses liposomes comprising, in addition to the PE, at least one other lipid, such as phospholipidic vesicles, including phosphatidylcholine (PC). (cols. 2 and 10).

Applicant's instantly claimed invention discloses known lexitropsins in a release system, which release system, as evidenced by the logic above, has been considered since at least the year 2000, or 2001 at the latest.

The level of ordinary skill in the pharmacological arts is extremely high. Because of the high level of skill and predictability of the pharmacological arts, a PHOSITA would find Applicant's invention obvious in light of the references mentioned, as well as Applicant's admission that lexitropsins are known for the treatment of viral, bacterial, and protazoarian infections.

Claim Rejections – 112, ¶2

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and **4** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, Claim 1 is indefinite as it recites the following phraseology, "A phospholipidic preparation consisting *in a release system and a lexitropsin. . .*" This phrase is grammatically incorrect. It is assumed Applicant means, "A phospholipidic preparation consisting**,** *in a release system***,** **<u>of</u>** *a lexitropsin. . .*" (Note: Commas before and after "in a release system", and "of" have been added, each underlined and bolded).

Regarding **Claims 1** and **4**, the phrases "*preferably*" and "*such as*" render the claims indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 6 recites the limitation "active principle". There is insufficient antecedent basis for this limitation in the claim, since **Claims 1-5** make no mention of "active principle".

Claim 8 provides for the "*use of the preparations of claims 1-7. . .*", but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 8 is also rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112 ¶1

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 8 is rejected under 35 U.S.C. § 112, first paragraph, because the claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the

invention.. Specifically, the Specification does not enable a PHOSITA to use the claimed preparations to treat *every* viral, bacterial, and protozoarian infection.

Therefore, the Specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. As stated in the MPEP 2164.01(a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is 'undue'."

In re Wands, 8 USPQ2d 1400 (1988), discusses the following factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph:

1. The nature of the invention;
2. The state of the prior art;
3. The predictability or lack thereof in the art;
4. The amount of direction or guidance present;
5. The presence or absence of working examples;
6. The breadth of the claims;
7. The quantity of experimentation needed; and
8. The level of skill in the art

The nature of the invention

Claim 8 is drawn to a method of treating every viral, bacterial, and protozoarian infection in any host.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art, namely pharmacology, involves screening *in vitro* and *in vivo* to determine if the compounds exhibit desired pharmacological activities, which are then tested for their efficacy on human beings. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. The instantly claimed invention is highly unpredictable in terms of the treatment of every viral, bacterial, and protozoarian infection.

As stated, pharmacology is an unpredictable art, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the claimed invention is highly complex, and one skilled in the art may recognize the claimed compounds as antiviral, antibacterial, and antiprotozoarian in respect to certain viruses, bacteria, and protozoa (either directly or peripherally within the mechanism of action) in assays. However, such properties do not mean that the same group of compounds and compositions may treat every type of viral, bacterial, and protozoarian infection.

The state of the prior art is silent as to whether Applicant's claimed genus of compounds is capable of treating both gram-positive and gram-negative bacterial infections, every virus known to man, nor every protozoa known to man.

The amount of direction or guidance present and the presence or absence of working examples

There is no direction or guidance presented which substantiates Applicant's claimed compounds as capable of treating every type of viral, bacterial, and protozoarian infection. No *in vivo* or *in vitro* data has been provided to support the scope of the instant claims.

The breadth of the claims, quantity of experimentation, and level of skill in the art

Claim 8 encompasses treating every type of viral, bacterial, and protozoarian infection in any host. In order to treat a disease, one would need to demonstrate what the subject population is, what the necessary dose is for efficacy, and that the subject has recovered from such a disease. Because of the aforementioned reasons, a person of skill in the art could not practice the claimed invention herein, or a person of skill in the art could practice the claimed invention herein only with undue experimentation and with no assurance of success.

Objections

Claims 2-8: Dependent upon rejected base claims.

Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of **Claim 1**. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Specifically, the structure disclosed in **Claim 5** is not supported by the genus depicted in **Claim 1**, from which **Claim 5** depends.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael P. Barker whose telephone number is (571) 272-4341. The examiner can normally be reached on Monday-Friday 8:00 AM- 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699. The unofficial fax phone for this group are (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is viable through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PRIMARY EXAMINER

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